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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/383,916	08/26/1999	DARRELL R. ANDERSON	012712-792	7181

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PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	21

DATE MAILED: 10/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/383916	Applicant(s) ANDERSON
	Examiner GAMBEL	Art Unit 1644

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 1/10/01; 8/6/01

2a)☐ This action is FINAL. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 41-55

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 41-55

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 8/6/02 (Paper No. 20), has been entered.

Applicant's amendment, filed 1/10/02 (Paper No. 14), has been entered.
Claims 21-40 have been canceled.
Claims 41-55 have been added.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 1/10/02 (Paper No. 14)
The rejections of record can be found in the previous Office Actions (Paper Nos. 9/13/16).

3. Claims 41, 42 and 44-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

Applicant is invited to provide objective evidence to support the predictability of treating autoimmune conditions with B7-specific antibodies consistent with and commensurate in scope with the claimed methods.

The following of record is set forth for applicant's convenience.

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of Immunosuppressive drugs such as costimulatory molecule-specific inhibitors can be species- and model-dependent, it is not clear that reliance on the experimental observations with the use of certain CD28:B7-specific inhibitors in certain in vitro and in vivo settings accurately reflects the relative efficacy of the claimed therapeutic strategy to treat any autoimmune condition with B7-specific antibodies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has argued in conjunction with U.S. Patent No. 5,885,579 that ligands to B7 may be used in therapeutic methods wherein the inhibition of the interaction of a B7 antigen with CD28 is therapeutically desirable.

In contrast to applicant's assertions, the examiner was not raising doubts about the validity of a U.S. Patent.

While applicant focused on the validity of in vitro assays for the efficacy of potential in vivo immunosuppressants; applicant was reminded that the claimed methods are drawn to treating autoimmune disorders with therapeutically effective amounts of B7.1- / CD80-specific antibodies.

Applicant argued in conjunction with U.S. Patent No. 6,162,432 that methods of treating skin disease including psoriasis with antibodies that inhibit LFA-3/CD2 interactions and other patents drawn to treating autoimmune diseases have been based on the ability to inhibit T cell activation and/or proliferation.

Applicant traversed the reliance upon Blazar et al, Perrin et al. and Daikh et al. to establish the problems and unpredictability of using B7-specific antibodies to treat autoimmune disorders and other diseases.

Applicant argued that Liu et al. (Digestive disease Week, May 21-24, 2000; #A583) supports the ability of anti-B7.1 antibodies, in contrast to anti-CTLA-4 and anti-B7.2 antibodies, to treat autoimmune responses in an animal model of colitis.

These observations by Liu et al. are consistent with the differences between targeting different members of the CD28-B7 pathway in the treatment of different autoimmune diseases.

The following of record was reiterated for applicant's convenience

Blazar et al. (J. Immunol. 157: 3250-3259, 1996) disclose that anti-CD80 or anti-CD86 antibodies were ineffective in preventing T cell CD8-mediated GVHD lethality; that each antibodies was partially effective in CD4-mediated GVHD lethality and that the combination of anti-CD80 and anti-CD86 antibodies were effective in preventing GVHD lethality in murine experimental models (see entire document, including the Abstract)

Perrin et al. (J. Neuroimmunol. 65: 31-39,1996) disclose that in contrast to the effective treatment of disease with CTLA-4 Ig; anti-CD80 (B7-1) attenuated the first clinical disease episode but not the relapse, anti-CD86 (B7-2) had no significant effect on the course of disease, and the combined treatment with anti-CD80 plus anti-CD86 resulted in the exacerbation of disease (see entire document). It is also noted that CTLA-4 Ig had a marked but incomplete therapeutic effect in the EAE model.

In addition, Yi-qun et al. (Intl. Immunol. 8: 37-44, 1996) disclose that their findings have a number of important implications for therapeutic approaches (see entire document, particularly Discussion, last paragraph). It is clear that inhibition of T cell response to soluble antigens will require the blocking of both B7-2 and B7-1 to be effective. More, important it is unlikely that ongoing T cell response will be susceptible to inhibition by anti-B7 reagents, for example in autoimmune diseases.

Daikh et al. (J. Leukoc. Biol. 62: 156-162, 1997) disclose that the role of CD28-B7 interactions are complex in autoimmune diseases and that B7-1-specific antibodies can exacerbate disease in an experimental model of diabetes (see pages 159-160, Effects of Selective Blockade of B7-1 of B7-2 on Autoimmunity).

Also, it is noted that targeting colitis with B7-1-specific antibodies, does not appear in the specification as-filed.

As pointed out previously, immunosuppression and inhibition of immune disorders are much easier to achieve under controlled in vitro conditions that experienced in the human immunoregulatory diseases targeted by the claimed invention. Here, the reliance upon observations wherein the B7-CD28 inhibitor antagonists are administered at the same time as initial stimulus or insult in experimental models are acknowledged. Even though subsequent secondary responses may be affected, such observations still rely upon inhibiting activation of B7-CD28 interactions at the onset or initiation of experiencing the antigen or stimulus and not upon experiencing an ongoing responses wherein secondary responses or antigen experienced lymphocytes are already in place. In contrast, the claimed methods encompass using B7-1 specific antibodies to treat autoimmune diseases wherein the diagnosis of such diseases occur after antigen priming has occurred.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective costimulatory-based therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for inhibiting any autoimmunity with B7-1-specific antibodies alone.

Applicant's arguments have not been found persuasive.

It was noted that treating psoriasis with B7-1-specific antibodies is considered enabled.
See Gottlieb et al., Journal of Investigative Dermatology 114(4): 840, (2000); Abstract # 546.

5. Applicant's cancellation of previous claims and submission of new claims in the amendment, filed 1/10/02 (Paper No. 14), has obviated the previous rejections under 35 USC 112, first and second paragraphs, with respect to deposit of biological materials and indefiniteness with respect to the recitation of "16C10, 7C10, 20C9 and 7B6".

6. Claims 41 and 44-55 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 41 and 44-55 are indefinite in the recitation of "a method of treatment that comprises blocking the B7.1/CD28 interaction in a subject in need of such treatment" because the metes and bounds of such treatment is ambiguous and indefinite. There is an absence or lack of clarity as to critical or key therapeutic endpoints which reads back on the preamble of the claimed methods

Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

7. As pointed out previously, applicant's submitted claims drawn to methods employing the 7C10, 7B6 and 16C10 specific antibodies appear free of the prior art. Therefore, applicant's newly added claims read on B7-specific antibodies that appear to be free of the prior art.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
October 21, 2002